EXHIBIT J

Trocar-Guided Transvaginal Mesh Repair of Pelvic Organ Prolapse

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OBJECTIVE: To prospectively assess clinical outcomes after pelvic organ prolapse repair with a standardized trocar-guided surgical device using polypropylene mesh.

METHODS: This was a prospective multicenter cohort study performed throughout 26 clinics. Evaluation at baseline, 2 months, and 1 year after surgery included prolapse grading using the pelvic organ prolapse quantification system (POP-Q) and symptom assessment using the Incontinence Impact Questionnaire (IIQ-7) and Urogenital Distress Inventory (UDI-6). For the purpose of this study, postoperative POP-Q stage 0–I was considered anatomic cure.

RESULTS: Two-hundred sixty-one patients were included in the study; 232 (89%) attended the 1-year follow-up. Mean±standard deviation age at surgery was 66.3±9.4 years. Anatomic cure 1 year after surgery was observed in 96 of 121 women (79%) after anterior repair with mesh ($P<.001$), and 56 of 68 (82%) after posterior repair with mesh ($P<.001$). For combined anterior and posterior mesh repair, cure was 51 of 63 (81%) and 54 of 63 (86%) for the anterior and posterior compartment, respectively ($P<.001$ for both). Bladder and rectal perforations occurred in 9 of 252 patients (3.4%). Vaginal erosions, the majority mild to moderate, occurred in 26 of 232 cases (11%). Surgical intervention due to mesh exposure occurred in seven cases (2.8%). There were significant quality-of-life improvements in all domains of the IIQ-7. Despite significant improvements in UDI-6 scores, symptoms specific for stress urinary incontinence were not ameliorated.

CONCLUSION: Trocar-guided transvaginal mesh surgery for pelvic organ prolapse is associated with satisfactory objective and subjective outcomes 1 year after surgery.

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See related article on page 127.

*For the other members of the Nordic Transvaginal Mesh Group who participated in this study, see the Appendix online at http://links.lww.com/A618.

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The rapid and widespread transition from traditional pelvic organ prolapse surgery to surgical techniques using biomaterials aims to improve on the often unsatisfactory surgical outcomes after prolapse corrective surgery.[1] The increased use of synthetic and biologic implants in pelvic reconstructive surgery is also influenced by the successful use of biomaterials in stress urinary incontinence surgery.[2,3]

When used for the tension-free vaginal tape (TVT) procedure, macroporous, monofilament, polypropylene mesh has shown advantageous properties as compared with other synthetic biomaterials.[4,5] As a result, polypropylene mesh has become the most commonly marketed biomaterial also for use in pelvic organ prolapse surgery. However, increasing the surface size and adding points of fixation may alter the

biomechanical characteristics of the mesh. The favorable outcomes associated with the use of polypropylene mesh for the TVT procedure can therefore not be assumed for other areas of pelvic surgery. Due to the lack of clinical safety and efficacy data, the adoption of polypropylene mesh for pelvic organ prolapse surgery remains a source of controversy.[6–8]

It has been suggested that in order for biomaterials to provide the intended pelvic floor support, they need to be "anchored" outside the afflicted tissues.[9] This has given rise to trocar-guided transvaginal surgical techniques using a transobturator or transgluteal approach, passing the mesh fixation arms through the arcus tendineus fascia pelvis or the sacrospinous ligaments.[9] Studies on perioperative morbidity and short-term clinical outcomes using trocar-guided mesh kits have yielded promising objective and subjective clinical outcomes.[10–13] However, many important long-term outcome measures have not yet been accounted for. This prospective multicenter cohort study aims to prospectively assess 1-year clinical outcomes after pelvic organ prolapse repair with a standardized trocar-guided surgical device using polypropylene mesh.

MATERIALS AND METHODS

We performed a prospective multicenter cohort study on the use of trocar-guided transvaginal mesh for pelvic organ prolapse. Patients with symptomatic pelvic organ prolapse were recruited at 26 centers in Sweden, Denmark, Finland, and Norway from June 2006 through March 2007. The study was approved by the appropriate research ethics committees in the participating countries. All patients underwent a standardized trocar-guided transvaginal mesh procedure using the Prolift system (Ethicon, Somerville, NJ). The compartment-specific surgical techniques have been described elsewhere,[9,12] and no alterations to the previously published surgical technique were allowed. Pelvic surgeons participating in the trial had supervised hands-on training in operating room sessions before initiation of the study and had participated in a previous cross-sectional study on the perioperative morbidity associated with the technique.[10] Decisions to perform concurrent stress urinary incontinence surgery were left to the discretion of the surgeon. We used 3-0 polyglactin 910 delayed absorbable sutures during the procedures. Administration of intraoperative antibiotics (metronidazole 1g intravenously and cephalosporin 1.5 g intravenously) was prescribed for patients included in the study, as was the change of gloves before handling the mesh and the use of surgical masks for operating room staff. Cystoscopy was not routinely used intraoperatively. Menopausal patients received preoperative topical estrogen treatment for 6–8 weeks before surgery and reinitiated the topical estrogen treatment after the 2-month follow-up visit for the duration of the trial.

In the clinic, before undergoing pelvic organ prolapse surgery, all patients underwent a physical examination, including a gynecological examination in the supine position using the pelvic organ prolapse quantification system (POP-Q). Methods, definitions, and descriptions conformed to the standards recommended by the International Continence Society.[14] Pelvic organ prolapse quantification system examinations were performed by a physician other than the operating gynecologist where available. For the purpose of this study postoperative POP-Q stage 0–I was considered anatomic cure, whereas postoperative POP-Q stage II or more in a repaired vaginal compartment was considered a surgical failure.

The gynecologic examination also included a macroscopic grading of vaginal inflammatory response on an ordinal scale.[15] Using a grading from 0–4 (0=none, 1=mild, 2=moderate, 3=pronounced, and 4=severe) the following clinical measures were assessed: granuloma, erosion, necrosis, infection, and rejection. Although not formally validated for urogynecologic surgery, the macroscopic inflammatory grading system has proven reliable and easy to use and has shown consistency with histopathologic assessments in a previous study on the use of biomaterials in pelvic reconstructive surgery.[16] The inflammatory assessment was completed by the postoperative examiner at baseline, two months, and 1 year postoperatively.

Patients completed the Incontinence Impact Questionnaire (IIQ-7) and the Urogenital Distress Inventory (UDI-6) preoperatively, at the 2 month, and 1-year follow-up. The IIQ-7 and UDI-6 are short-form validated questionnaires,[17–19] which were translated without formal validation to the language of each country. The Swedish version was formally language validated and found to have satisfactory correlation with the English version (data not shown). Response alternatives are based on a four-point Likert scale (0=not at all; 1=slightly; 2=moderately; 3=greatly). The IIQ-7 is designed to assess the effect of urinary incontinence on activities and emotions in the quality of life of women, and the UDI-6, to assess the degree to which symptoms associated with incontinence are troubling. Both short-form questionnaires have been validated and proven responsive to change after pelvic reconstructive surgery.[20] Scores on the IIQ-7 and UDI-6 were calculated in a simple additive fashion,[21] where a higher score indicates more incon-

tinence and distressful symptoms (maximum score 21 for the IIQ and 18 for the UDI).

Inclusion criteria included fluency in the respective countries' language; POP-Q stage II or more; and symptoms specifically attributed to pelvic organ prolapse, including vaginal bulging, pelvic heaviness, or vaginal protrusion. All patients had to be able to give informed consent to participate and were required to be physically and mentally able to participate in follow-up. Exclusion criteria included any previous pelvic organ cancer, severe rheumatic disease requiring per oral steroid treatment, systemic connective tissue disorders, and patients physically or mentally unable to participate in follow-up or give informed consent to participate in the study.

Baseline patient characteristics, demographic data, and medical history were collected using a standardized questionnaire. A standardized protocol was used to describe the surgical procedures, the associated hospital stay, and patients' medical history. All trial protocols were submitted to the clinical research unit at the Department of Obstetrics and Gynecology, Danderyd University Hospital, Stockholm, Sweden, and only the principal investigators had access to the data. The transvaginal mesh manufacturing company had no influence over study aim, study design, execution of the study or analysis, or interpretation of data. The corresponding author guarantees the integrity of the data, drafted the paper, and had the final responsibility for the decision to submit for publication.

Data on patient and surgical characteristics are presented as frequency (%). Results from the IIQ-7 and UDI-6 questionnaires are presented as calculated scores and frequencies. Comparisons on ordinal data between baseline and the 2-month and 1-year assessment were performed using the nonparametric Wilcoxon signed rank test for dependent samples. Comparisons between proportions were performed using the χ^2 test. All analyses were performed using Statistica software (StatSoft, Inc., Tulsa, OK), and a $P<.05$ was considered significant for all analyses.

RESULTS

During the study period, a total of 261 patients were included, of which nine patients were excluded due to missing information. The 2-month visit was attended by 243 (93%) patients, and 232 (89%) patients attended the 1-year follow-up. Mean±standard deviation age at surgery was 66.3±9.4 years, mean body mass index (BMI) was 26.7±4.0 and median parity was 2 (range 0–7). The majority of patients had undergone at least one previous pelvic operation, and trocar-guided transvaginal mesh surgery was performed as a secondary procedure in a total of 128 (50.8%) patients, as indicated by the number of patients who had undergone previous traditional prolapse surgery. Detailed cohort demographics are presented in Table 1.

Surgical characteristics are presented in Table 2. Anterior repair with mesh was performed in 121 of 261 patients (48%), posterior repair with mesh in 68 of 261 patients (27%) and combined anterior–posterior procedures in 63 of 261 patients (25%). Concurrent surgeries were performed in 34 patients (13%), the most common procedures being posterior colporrhaphy and perineorrhaphy at the time of anterior transvaginal mesh repair. The most common perioperative serious complications were bladder and rectal perforations, which occurred in a total of nine patients (3.4%). There was one case of serious perioperative bleeding (1,500 mL) during a combined anterior and posterior procedure. The profuse bleeding was managed on the operating table after suture ligation and compression. There was only one more bleeding in excess of 500 mL observed. Minor surgical complications were dominated by urinary retention, urinary tract infections, and groin/buttock pain (Table 2).

Anatomic outcomes and POP-Q characteristics are presented in Table 3. For anterior mesh repair, overall anatomic cure was observed in 98 of 121 patients (81%) after 2 months and 96 of 121 (79%) after 1 year ($P<.001$ for both in comparison to baseline). For posterior mesh repair, anatomic cure was reported in 58 of 68 patients (85%), and 56 of 68 patients (82%) at 2 months and 1 year follow-up, respectively ($P<.001$ for both in comparison to baseline). For the combined anterior and posterior mesh procedure, anterior compartment cure was achieved in 52 of 63 (83%) and 51 of 63 (81%) at 2 months and 1 year follow-up, respectively ($P<.001$ for both in comparison to baseline), whereas posterior compartment anatomic cure was achieved in 55 of 63 (87%) and 54 of 63 (86%) at 2 months and 1 year follow-up, respectively ($P<.001$ for both in comparison to baseline). There was an overall tendency toward lesser prolapse severity in the middle compartment, with the most prominent prolapse reduction noticed in point C and D after posterior repair ($P<.001$) and combined anterior–posterior repair ($P<.001$). Tvl and points Gh and Pb, showed minor and nonsignificant variations over time, regardless of surgical technique (Table 3).

Macroscopic inflammatory assessments are presented in Table 4. In comparison with baseline, all inflammatory measures increased postoperatively. Granuloma formation and signs of rejection dropped

Table 1. Patient Characteristics

	Anterior Repair (n=121)	Posterior Repair (n=68)	Anterior and Posterior Repair (n=63)
Age (y)	66.0±8.4	66.7±10.2	66.3±10.4
Parity	2 (0–5)	2 (0–6)	3 (0–7)
Body mass index	27.1±4.2	26.3±4.1	26.1±3.6
Educational level			
Compulsory school	81 (67)	34 (50)	25 (40)
High school	23 (19)	16 (24)	19 (30)
College/university	15 (12)	13 (19)	12 (19)
Annual income (€)			
Less than 10,000	22 (18)	12 (18)	10 (16)
10,000–30,000	77 (64)	25 (37)	24 (38)
30,000–40,000	5 (4)	12 (18)	5 (8)
More than 40,000	2 (2)	4 (6)	1 (2)
Smoker			
Yes	9 (7)	9 (13)	6 (10)
No	111 (92)	58 (85)	54 (86)
Menopausal			
Yes	110 (91)	59 (87)	55 (87)
No	4 (3)	4 (6)	2 (3)
Hormone replacement therapy			
Local	49 (40)	22 (32)	21 (33)
Systemic	33 (27)	19 (28)	13 (21)
Somatic diseases			
Cardiovascular disease	52 (43)	26 (38)	34 (54)
Thyroid dysfunction	16 (13)	8 (12)	8 (13)
Asthma	9 (7)	6 (9)	5 (8)
Arthrosis	6 (5)	6 (9)	4 (6)
Diabetes	4 (3)	3 (4)	4 (6)
Previous pelvic surgery			
Hysterectomy	55 (45)	37 (54)	39 (62)
Prolapse	73 (60)	32 (47)	23 (37)
Incontinence	8 (7)	9 (13)	6 (10)
Salpingo-oophorectomy	27 (22)	22 (32)	10 (16)
Other	9 (7)	8 (12)	3 (5)

Data are mean±standard deviation, median (range), or n (%).

after an initial increase in prevalence, but the number of erosions increased to 26 of 232 cases (11%, 95% confidence interval 7.2–15.3%) 1 year after surgery. There was no increase of mesh-related infections at 1 year compared with baseline. The median severity score was 0 for all measures throughout the study, and most cases of reaction to the mesh were in the range of mild-to-moderate reactions. Although no cases of severe inflammatory reactions were reported, the need to cover or remove exposed mesh during the postoperative period occurred in seven cases (2.8%, 95% confidence interval 0.8–5.2), five after anterior mesh repair and two after posterior repair. The remaining cases were all managed conservatively using topical estrogen or antibiotic cream.

Detailed outcomes of the IIQ-7 and UDI-6 questionnaires are presented in Tables 5 and 6. There were significant postoperative quality-of-life improvements in all aspects of the IIQ-7. One year after surgery, improvements in overall IIQ-7 scores were similar for the various surgical techniques (Table 5). After anterior repair, improvements in specific UDI-6 questions were observed for symptoms of "urinary frequency," "urgency incontinence," "bladder emptying difficulties" and "pain in the lower abdomen." However, for symptoms of "urine leakage related to physical activity" and "small amounts of urine leakage," the changes were not at a significant level. A total of five participants (2%) underwent stress urinary incontinence surgery during the follow-up period (these cases were excluded from analysis of UDI-6 scores). A similar but less pronounced pattern of improvement for lower urinary tract symptoms was observed in women after combined anterior–posterior repair, as well as in women with isolated posterior repair. The overall UDI-6 scores were similar for the various surgical techniques and significantly lower compared with preoperative scores (Table 6).

Table 2. Surgical Characteristics and Adverse Events Associated With Transvaginal Mesh Repair Using the Prolift System

	Anterior Repair (n=121)	Posterior Repair (n=68)	Anterior and Posterior Repair (n=63)
Operating time (min)	59.7±20.2	54.4±18.6	96±36.9
Antibiotic prophylaxis	116 (95.9)	66 (97.1)	60 (95.2)
Bleeding (mL)	103.4±110.2	52.8±55.6	168.5±216.8
Concurrent surgery			
Hysterectomy	3 (2.5)	0 (0)	5 (7.9)
Anterior colporrhaphy	NA	2 (2.9)	NA
Posterior colporrhaphy	8 (6.6)	NA	NA
TVT/TVT-O	1 (0.8)	1 (1.5)	1 (1.6)
Sacrospinous fixation	3 (2.5)	0 (0)	0 (0)
Cervix amputation	1 (0.8)	0 (0)	0 (0)
Perineorrhaphy	6 (5)	6 (8.8)	4 (6.3)
Anesthesia			
Local	9 (7.4)	6 (8.8)	2 (3.2)
Epidural	1 (0.8)	2 (2.9)	1 (1.6)
Spinal	69 (57)	45 (66.2)	38 (60.3)
General	39 (32.2)	13 (19.1)	17 (27)
Perioperative catheter	105 (86.8)	55 (80.1)	58 (92.1)
Postoperative vaginal tamponade	89 (73.6)	44 (64.7)	44 (69.8)
Hospital stay (d)	2 (0–15)	2 (0–7)	2 (0–13)
Complications			
Bleeding requiring transfusion	0 (0)	0 (0)	1 (4.8)
Bladder perforation	6 (5)	0 (0)	2 (3.2)
Rectal perforation	0 (0)	0 (0)	1 (1.6)
Urinary tract infection	4 (3.3)	2 (2.9)	3 (4.8)
Bladder retention	11 (9.1)	3 (4.4)	5 (7.9)
Groin/buttock pain	3 (2.5)	1 (1.5)	1 (1.6)
Vaginal hematoma	1 (0.8)	2 (2.9)	2 (3.2)
Cardiovascular disease	6 (5)	2 (2.9)	2 (3.2)

NA, not applicable; TVT, tension-free vaginal tape; TVT-O, transobturator tension-free vaginal tape.
Data are mean±standard deviation, n (%), or median (range).
Variables not adding up to 100% represent missing values.

DISCUSSION

In recent years, material innovations and improved biocompatibility have revived interest in the use of biomaterials in prolapse surgery, with expectations of results similar to the successful use of implants in stress urinary incontinence surgery. However, compelling clinical evidence demonstrating that their use improves outcomes compared with traditional suture techniques is lacking.

The present 1-year prospective cohort study suggests that trocar-guided transvaginal mesh surgery for

Table 3. Distribution of Pelvic Organ Prolapse Quantification Values Preoperatively and Postoperatively

	Anterior Repair			Posterior Repair			Anterior and Posterior Repair		
	Preoperatively	2 Mo	1 Y	Preoperatively	2 Mo	1 Y	Preoperatively	2 Mo	1 Y
Anterior									
Aa	1 (–1 to 4)	–3 (–4 to 0)	–2 (–3 to 2)	–3 (–3 to 0)	–3 (–4 to 1)	–3 (–4 to 1)	1 (–2 to 5)	–3 (–3 to 0)	–3 (–4 to 0)
Ba	2 (–1 to 7)	–3 (–3 to 0)	–2 (–4 to 3)	–2 (–3 to 1)	–3 (–4 to 1)	–2 (–3 to 1)	2 (–1 to 8)	–3 (–3 to 0)	–2 (–4 to 0)
Stage	II (II–IV)	I (0–II)	I (0–III)	I (0–II)	I (0–II)	I (0–II)	II (II–IV)	I (0–II)	I (0–II)
Middle									
C	–1 (–1 to –9)	–6 (–11 to –5)	–6 (–10 to –4)	–3 (–9 to 9)	–6 (–11 to –5)	–6 (–11 to –4)	2 (–10 to 8)	–7 (–10 to –5)	–6 (–12 to –4)
D	–7 (–10 to –3)	–7 (–12 to –5)	–7 (–10 to –4)	–6 (–12 to 0)	–7 (–12 to –6)	–7 (–12 to –4)	–6 (–12 to 0)	–8 (–11 to –6)	–7 (–11 to –6)
Stage	I (0–II)	I (0–I)	I (0–II)	I (0–IV)	I (0–II)	I (0–II)	II (0–IV)	I (0–II)	I (0–II)
Posterior									
Ap	–2 (–4 to 0)	–3 (–4 to 0)	–2 (–3 to 1)	1 (–2 to 5)	–3 (–3 to 3)	–3 (–3 to 3)	1 (–2 to 5)	–3 (–3 to 0)	–3 (–3 to 3)
Bp	–2 (–3 to 0)	–2 (–3 to 0)	–2 (–3 to 2)	2 (–1 to 5)	–3 (–3 to 3)	–3 (–3 to 3)	2 (–1 to 8)	–3 (–3 to 2)	–3 (–3 to 3)
Stage	I (0–II)	I (0–II)	I (0–II)	III (II–IV)	I (0–III)	I (0–III)	II (II–IV)	I (0–III)	I (0–III)
Gh	5 (1–7)	4 (2–8)	4 (3–7)	5 (3–8)	4 (2–7)	4 (2–6)	5 (3–9)	4 (3–8)	4 (3–8)
Pb	3 (2–7)	3 (2–6)	3 (2–6)	4 (2–6)	4 (2–6)	4 (2–6)	4 (2–8)	4 (2–7)	4 (2–7)
Tvl	8 (6–12)	8 (6–11)	8 (5–13)	8 (5–12)	8 (5–12)	8 (5–13)	9 (5–12)	8 (5–12)	9 (5–13)

Data are median (range).

Table 4. Macroscopic Assessment of Clinical Inflammatory Reaction to Transvaginal Mesh

	Preoperatively (n=252)		2 Mo (n=243)			1 Y (n=232)		
	No. of Cases (%)	Median Severity (Range)	No. of Cases (%)	Median Severity (Range)	*P*	No. of Cases (%)	Median Severity (Range)	*P*
Total	13 (5)		128 (53)		<.001	65 (28)		<.001
Granuloma	3 (1)	0 (0–2)	73 (30)	0 (0–3)	<.001	19 (8)	0 (0–2)	<.001
Erosion	6 (2)	0 (0–3)	16 (7)	0 (0–2)	.02	26 (11)	0 (0–3)	.001
Necrosis	1 (1)	0 (0–1)	11 (5)	0 (0–2)	.003	12 (5)	0 (0–2)	.001
Infection	3 (1)	0 (0–1)	10 (4)	0 (0–2)	.04	4 (2)	0 (0–2)	.62
Rejection	0 (0)	0 (0–2)	18 (7)	0 (0–2)	<.001	4 (2)	0 (0–2)	.04

Statistical comparison with preoperative values for 2-month and 1-year follow-up using the Wilcoxon signed rank test. There were no cases of de novo granuloma formation between the 2-month and 1-year assessment.

pelvic organ prolapse is associated with satisfactory subjective and objective clinical outcomes. The overall anatomic cure rates ranged between 79% and 86%, with sustainability of pelvic organ support for a 1 year follow-up period. In comparison with isolated procedures, combined anterior and posterior transvaginal

Table 5. Outcomes of the Short-Form Incontinence Impact Questionnaire

	Anterior Repair (n=121)		Posterior Repair (n=68)		Anterior and Posterior Repair (n=63)	
	Preop	1 Y	Preop	1 Y	Preop	1 Y
How does incontinence affect your						
Household chores		*P*<.001		*P*<.001		*P*=.002
Not at all	76 (63)	92 (76)	43 (63)	55 (81)	36 (57)	49 (78)
Slightly-moderately	34 (28)	12 (10)	17 (25)	6 (13)	21 (33)	8 (13)
Greatly	4 (3)	1 (1)	4 (6)	0 (0)	3 (5)	1 (2)
Physical recreation		*P*<.001		*P*<.001		*P*<.001
Not at all	57 (47)	82 (68)	30 (44)	43 (63)	31 (49)	43 (68)
Slightly-moderately	44 (36)	24 (20)	24 (35)	16 (24)	22 (35)	14 (22)
Greatly	10 (8)	1 (1)	6 (9)	2 (3)	6 (10)	0 (0)
Entertainment activities		*P*<.001		*P*=.02		*P*=.02
Not at all	75 (62)	94 (78)	37 (54)	46 (68)	37 (59)	48 (76)
Slightly-moderately	31 (26)	11 (9)	16 (23)	11 (16)	13 (21)	9 (14)
Greatly	5 (4)	1 (1)	7 (10)	3 (4)	6 (10)	0 (0)
Ability to travel by car/bus more than 20 min		*P*=.002		*P*=.05		*P*<.001
Not at all	80 (66)	94 (78)	43 (63)	49 (72)	42 (67)	51 (81)
Slightly-moderately	29 (24)	10 (8)	12 (10)	10 (15)	14 (22)	7 (11)
Greatly	5 (4)	0 (0)	6 (9)	0 (0)	4 (6)	0 (0)
Social activities		*P*<.001		*P*=.02		*P*=.002
Not at all	74 (61)	90 (74)	37 (54)	51 (75)	35 (56)	46 (73)
Slightly-moderately	34 (28)	14 (12)	15 (22)	6 (13)	17 (27)	9 (14)
Greatly	5 (4)	0 (0)	5 (7)	3 (4)	6 (10)	1 (2)
Emotional health		*P*=.002		*P*=.01		*P*=.01
Not at all	82 (68)	89 (74)	40 (59)	52 (76)	38 (60)	41 (65)
Slightly-moderately	28 (24)	13 (11)	13 (19)	7 (10)	14 (22)	13 (21)
Greatly	2 (2)	0 (0)	3 (4)	0 (0)	6 (10)	2 (3)
Feeling frustrated		*P*<.001		*P*<.001		*P*<.001
Not at all	69 (57)	91 (75)	30 (44)	48 (71)	30 (48)	45 (71)
Slightly-moderately	37 (31)	13 (11)	21 (31)	11 (16)	17 (27)	12 (19)
Greatly	5 (4)	0 (0)	5 (7)	0 (0)	9 (14)	0 (0)
Summated IIQ-7 score		*P*=.1		*P*=.05		*P*=.03
Mean±standard deviation	3.9±4.9	2.8±2.9	4.3±5.4	3.3±2.7	5.0±6.0	2.8±2.5

Preop, preoperative; IIQ-7, Incontinence Impact Questionnaire.
Data are n (%) unless otherwise specified.
Statistical comparison between preoperative values and 1-year follow-up used the Wilcoxon signed rank test.

Table 6. Outcomes of the Short-Form Urinary Distress Inventory

	Anterior Repair(n=121)		Posterior Repair(n=68)		Anterior and Posterior Repair(n=63)	
	Preop	1 Y	Preop	1 Y	Preop	1 Y
How bothersome are the following symptoms for you?						
Frequent urination		$P<.001$		$P=.03$		$P<.001$
Not at all	30 (25)	62 (51)	20 (29)	20 (29)	8 (13)	30 (48)
Slightly-moderately	58 (48)	46 (38)	29 (43)	41 (60)	33 (52)	28 (44)
Greatly	27 (22)	0 (0)	16 (24)	0 (0)	19 (30)	0 (0)
Urine leakage related to urgency		$P<.001$		$P=0.19$		$P=0.002$
Not at all	45 (37)	69 (57)	35 (51)	39 (57)	23 (37)	39 (62)
Slightly-moderately	50 (41)	47 (39)	19 (28)	23 (34)	26 (41)	20 (32)
Greatly	19 (16)	0 (0)	5 (7)	0 (0)	8 (13)	0 (0)
Urine leakage related to physical activity		$P=0.18$		$P=0.49$		$P=0.87$
Not at all	50 (41)	59 (49)	37 (54)	36 (53)	26 (41)	30 (48)
Slightly-moderately	59 (49)	39 (32)	18 (26)	21 (31)	27 (43)	25 (40)
Greatly	6 (5)	9 (7)	3 (4)	3 (4)	4 (6)	1 (2)
Small amounts of urine leakage		$P=0.08$		$P=0.98$		$P=0.17$
Not at all	77 (64)	78 (64)	44 (65)	46 (68)	38 (60)	44 (70)
Slightly-moderately	33 (27)	28 (23)	16 (24)	16 (24)	15 (24)	15 (24)
Greatly	3 (2)	0 (0)	0 (0)	0 (0)	3 (5)	0 (0)
Difficulty emptying bladder		$P<.001$		$P=0.02$		$P<.001$
Not at all	43 (36)	76 (63)	30 (44)	33 (49)	21 (33)	40 (63)
Slightly-moderately	57 (47)	25 (21)	25 (37)	27 (40)	28 (44)	15 (24)
Greatly	17 (14)	6 (5)	7 (10)	2 (3)	8 (13)	1 (2)
Pain lower abdomen or genital area		$P<.001$		$P=0.38$		$P=0.02$
Not at all	85 (70)	94 (78)	48 (71)	53 (78)	41 (65)	47 (75)
Slightly-moderately	24 (20)	13 (11)	9 (13)	8 (12)	14 (22)	8 (13)
Greatly	6 (5)	0 (0)	3 (4)	1 (1)	4 (6)	2 (3)
Summated UDI-6 score		$P<.001$		$P=0.03$		$P<.001$
Mean±standard deviation	5.4±3.9	2.9±2.7	4.4±2.3	3.3±2.7	5.9±3.8	3.0±2.6

Preop, preoperative; UDI-6, Urinary Distress Inventory.
Data are n (%) unless otherwise specified.
All statistical comparisons between preoperative values and 1-year follow-up used the Wilcoxon signed rank test.

mesh repair was associated with the most effective restoration of vaginal support. This could be explained by the synergistic support added to the upper vagina by anchoring mesh in both the anterior and the posterior compartment at the same time. Combined anterior and posterior mesh repair was also effective for the restoration of middle compartment support in cases of uterine or vaginal vault prolapse.

Normative data on pelvic organ support indicate that in women of geriatric age, nearly 60% have pelvic organ prolapse stage II as defined by the POP-Q.[22] In the present study we chose to define optimal surgical outcomes (ie, anatomic cure) as POP-Q stage 0-I, corresponding to the leading edge at maximum −2 at point Ba or Bp. Had we chosen an alternative, more generous definition of anatomic cure such as number of patients with the leading edge inside the hymen (corresponding to maximum −1 or less at point Ba or Bp), the surgical success would have exceeded 90% for all vaginal compartments. We opted for the stricter definition of surgical cure, which in combination with differences in study design, follow-up time, and prolapse classification system, could explain the lower cure rates of the present study when compared with the 95% overall success rate using the same surgical kit described by Fatton et al[12] The few concomitant pelvic surgical procedures add to the internal validity of our study and support a causal

relationship between transvaginal mesh surgery and effective restoration of pelvic organ support. We recognize that some degree of classification bias may have been introduced by not having access to an independent examiner for the postoperative POP-Q examinations at all study cites. All centers agreed not to perform any transvaginal mesh surgery outside the study during the inclusion period. yet the wide inclusion criteria could have introduced a certain degree of selection bias.

In comparison with studies using the POP-Q system to describe surgical outcomes in prolapse corrective surgery, our anatomic cure rates are superior to what previously has been reported for traditional anterior repair.[23–25] However, when compared with traditional posterior repair, the trocar-guided transvaginal mesh technique yielded similar anatomic outcomes to what has been reported using either colporrhaphy or midline plication.[24,26–28] Thus, it seems that with regard to restoration of pelvic organ support, the trocar-guided transvaginal mesh technique has its greatest advantage in anterior vaginal wall prolapse repair. Although we observed significant postoperative anatomic improvements also in the middle compartment, further studies using comparable outcome measures (POP-Q) are needed to determine how trocar-guided transvaginal mesh compares to uterine prolapse surgery using sacrocolpopexy or sacrospinous fixation.

Perhaps even more important than the satisfactory surgical outcomes were the major improvements in all quality-of-life domains measured by the IIQ-7. The change in better social functioning was reflected by less interference with physical activities, emotional health, social interactions, and physical recreation as soon as 2 months after surgery. The improvements were sustained for the duration of our study, although somewhat less pronounced at 1 year, compared with 2 months. Patient satisfaction may not correspond to anatomic outcomes, and the concept of cure in pelvic reconstructive surgery is under debate.[29,30] That said, our data nonetheless show that an efficacious reduction of prolapse severity is associated with rapid and persistent improvements in women's quality of life. The observed quality-of-life improvements were of a similar magnitude regardless of which vaginal compartment was repaired.

Most symptoms associated with lower urinary tract dysfunction improved significantly for the duration of follow-up irrespective of surgical technique. The improvements in overall scores were, however, less than 0.5 standard deviation of the baseline score, which has been suggested as an estimate of the minimally clinically important difference. Symptoms specific for stress urinary incontinence were not ameliorated to the same extent as other lower urinary tract symptoms. In terms of urethral physiology, it is possible that the trocar-guided transvaginal mesh procedure results in an overcorrection of anterior vaginal wall and bladder neck support, resulting in de novo symptoms or aggravation of preexisting symptoms of stress urinary incontinence. This was reflected in the need for stress urinary incontinence surgery in five women after the 2-month visit. An adverse effect on urethral function may not become apparent in studies where a large number of concomitant retropubic or transobturator incontinence procedures are performed at the time of transvaginal mesh surgery.[12,31]

In the present study, the number of surgical perioperative adverse events and rates of complication were comparable with previous reports.[10,31] However, when using surgical techniques involving permanent biomaterials, specific mesh-related complications, such as erosion and contraction, must be considered.[32] Polypropylene mesh contraction may be viewed upon as a "shrinkage" of the mesh due to fibrosis of the surrounding tissues rather than a diminution of the mesh itself.[33] Consistent measurements of transvaginal length throughout the study period suggest that at least longitudinal contraction and a clinically significant shortening of the vagina did not occur. A classification system that takes into account measurements of vaginal width is not available. We therefore could not determine whether the transvaginal mesh technique gives rise to a narrowing of the vagina.

To assess mesh-related adverse events, the study also included a longitudinal assessment of clinical inflammatory measures graded on a visual severity scale. The overall number of cases with any mesh-related reaction increased up to the 2-month follow-up postoperatively but subsequently declined up to the 1-year assessment. Preoperative observations of granuloma and mucosal erosion were attributed to some women wearing pessaries. Severe inflammatory reactions were uncommon, yet mild-to-moderate reactions were significantly increased 1 year after surgery. Contrary to the tendency of decreasing counts of granuloma, infection, and rejection, the prevalence of erosions increased 1 year after surgery and were observed in a total of 11% of our participants. Rates of mesh exposure and erosion in the range of 9–13% have been reported by other investigators,[34,35] but in contrast to these studies, the need for reoperation due to mesh erosion was lower in the present study. According to the protocol, all patients received standardized topical estrogen therapy preoperatively and

as of the 2-month follow-up visit. This may have had a positive effect on the prevalence and magnitude of inflammatory response, and the absence of severe erosions would indicate that such therapy is beneficial after transvaginal mesh repair.

Our multicenter study has demonstrated that standardized trocar-guided transvaginal mesh techniques can be performed in a multicenter setting with a relatively low rate of serious surgical complications and with satisfactory subjective outcomes after instructor-supervised hands-on training sessions. The uniform surgical technique, the condition-specific outcome measures, the multicenter setting, and the prospective data collection are some of the methodologic merits of our study. A near-90% patient compliance in follow-up further strengthens our study by minimizing selection and reporting bias. In this study, patients served as their own controls, but we recognize that an independent control group would have added a valuable dimension to the interpretation of our results. Randomized controlled trials are now needed to clarify how the risks and benefits associated with the use of synthetic mesh kits in prolapse surgery relate to patient satisfaction when compared with traditional prolapse repair.

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